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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,247	10/27/2003	Wayne Dawson	F-8015	5890

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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,247	DAWSON ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I in the reply filed on 29 September 2006 is acknowledged.

Claim Status

Claims 1-13 are pending.

Claims 1-11 and 13 are being examined.

Specification

Objection is made to the Title. It is suggested that the term novel be removed from the title.

Claim objections

Claims 8 and 13 are objected to because the steps of the claims are mislabeled. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the broad recitation of the "folding of a biopolymer", and the claim also recites protein folding which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). Claims 2-7 and 13 are also rejected because they depend from claim 1, and thus contain the above issues due to said dependence.

Regarding claim 5, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Claims 6-7 are also rejected because they depend from claim 5, and thus contain the above issues due to said dependence.

The term "computational manageable number" in claim 8 is a relative term which renders the claim indefinite. The term "computational manageable number" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What is a "computationally manageable number"? Claim 9-11 are also rejected because they depend from claim 8, and thus contain the above issues due to said dependence.

Claim 10 recites the limitation "the optimal β-sheet alignments" in the body of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 11 is also rejected because it depends from claim 10, and thus contain the above issues due to said dependence.

Claim Rejections - 35 USC § 112, 1st Paragraph

Claim 4-7 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for topology prediction/estimation, does not reasonably provide enablement for functional prediction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.
The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not

'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the instant case, claim 4 is directed to the prediction of loss of function biological activity based only on predicted protein topology. The specification does not provide the required guidance to support limitations of claim 4. The specification also fails to provide examples how the loss of biological function is predicted based on the estimated topology. The current state of the art teaches against the ability to estimate changes in a protein's functionality based on prediction of structure (Tosatto et al., Current Pharmaceutical Design, Vol. 12, 2067-2086, 2006). Tosatto et al. teach that the estimation of protein function based on the predicted structure is unpredictable. Specifically, Tosatto et al teach that although two protein share common structure, common function cannot be predicted. In some case function may be shared, in others the proteins have different functions. Alternatively, two proteins could have different

structures and yet have the function. The correct evaluation of function predictions has been hindered by the lack of consistent and thorough experimental data concerning the biochemical properties of targets. Tosatto et al. teach that considerable new developments are still needed to disclose the rules governing the multiple facets of protein function (p. 2080, col. 1, lines 41-43). One of ordinary skill in the art would be required to perform undue experimentation to determine predictable rules and algorithms to make functional predictions based on predicted structure but also based only on topology as is instantly claimed. Claims 5-7 are also rejected as they depend from claim 4, and thus contain the above issues due to said dependence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 8, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Dawson et al. (J. theor. Biol., Vol. 213, p. 359-386, 2001).

Claim 1, 3 and 13 are drawn to a method to predict the topology of the spatial arrangement of an amino acid sequence using an entropy evaluation model that takes into account the global contributions of entropy to the folding of a biopolymer combined with other thermodynamic potentials as a protein folding model, in which the cross

linking entropy (CLE), which is an entropy evaluation model that takes into account the global effects of entropy in the folding of a biopolymer, is used to evaluate the entropy loss of a protein due to folding into a particular topology given a known secondary or estimated secondary structure. The method comprising the steps: A. obtaining an amino acid sequence of a protein; B. preparing information on the secondary structure of the said amino acid sequence by way of at least one theoretical or experimental estimate; C. applying the CLE method to approximate the global folding kinetics of the said amino acid sequence; D. using the global folding kinetics to predict the optimal topology of the said amino acid sequence; and E. storing the information in a data file or in other form of digital memory.

Dawson et al. teach a method to predict the topology of the spatial arrangement of an amino acid sequence using an entropy evaluation model that takes into account the global contributions of entropy to the folding of a biopolymer combined with other thermodynamic potentials as a protein folding model (p. 359, abstract), in which the cross linking entropy (CLE), which is an entropy evaluation model that takes into account the global effects of entropy in the folding of a biopolymer, is used to evaluate the entropy loss of a protein due to folding into a particular topology given a known secondary or estimated secondary structure (p. 365, col. 2, line 3-5). The method comprising the steps: A. obtaining an amino acid sequence of a protein; B. preparing information on the secondary structure of the said amino acid sequence by way of at least one theoretical or experimental estimate (p. 360, col. 1, para 3, lines 17-23); C. applying the CLE method to approximate the global folding kinetics of the said amino

acid sequence; D. using the global folding kinetics to predict the optimal topology of the said amino acid sequence (p. 378, col. 1, lines 1-3); and E. storing the information in a data file or in other form of digital memory (p. 376, table 2).

Regarding claim 8, Dawson et al. teach the equation $\Delta S_{i,j} = \frac{\gamma k_B}{\xi}\left[\ln\left(\frac{2\gamma\xi N_{i,j}}{3\lambda^2}\right) - 1 + \left(\frac{3\lambda^2}{2\gamma\xi N_{i,j}}\right)\right]$ (p.368, eqn 9), after the terms $\theta(\xi)=\frac{1}{\xi}$ (eqn. 8) and $\psi = \frac{2\gamma\xi}{3\lambda^2}$ are substituted into Eqn. 9. Further, it is well known in the art that $\Delta G = \Delta H - T\Delta S$ and Dawson et al. teach that the calculation total Gibb's free energy (p. 370, eqn. 16). Thus Dawson et al. teach the equation of claim 8.

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karlheinz R. Skowronek/
KRS

MICHAEL BORIN, PH.D
PRIMARY EXAMINER